Comm.
Dr. Bing
Dr. Loosli
Dr. Sommers

MISCELLANEOUS

#1932

THE COUNCIL FOR TOBACCO RESEARCH—U.S.A., INC.
110 EAST 59TH STREET
NEW YORK, N. Y. 10022
(212) 421-8885

JUL 30 1973

Application for Research Grant

Date: 7-20-73

(Use extra pages as needed)

1. Principal Investigator (give title and degrees):

W. LeRoy Heinrichs, M.D., Ph.D.
Professor, Department of Obstetrics and Gynecology
Director of Endocrine Research

2. Institution & address:

University of Washington
Seattle, Washington 98195

3. Department(s) where research will be done or collaboration provided:

Obstetrics and Gynecology, University of Washington
Pediatrics, University of Washington
Pharmacology, University of Washington
Anesthesiology, Harborview Medical Center, Seattle, Washington

4. Short title of study:

The Effect of Smoking on Adaptive Changes of Previable Human Pregnancies

5. Proposed starting date: January 1, 1974

6. Estimated time to complete: one year

7. Brief description of specific research aims:

The cardiopulmonary and metabolic-endocrine adaptations in the placental and fetal morphology and enzymology of women seeking termination of 14-16 week pregnancies will be compared in nonsmokers and in women smoking cigarettes or marijuana.

A. Cardiopulmonary studies; the cardiac output, peripheral resistance, arterial blood gases, tidal volume and minute volume will be determined one day preabortion and six weeks postabortion.

B. Metabolic-endocrine; blood lipid assays will include total cholesterol and esters, phospholipids and triglicerides. Plasma hormones will be HCG (human chorionic gonadotrophin), HCS (human chorionic somatomammotrophin), progesterone, and estradiol. In addition to routine preoperative assays, plasma carboxyhemoglobin concentrations will be ascertained.

C. Fetal morphology; the total body measurements, fetal organ and placental weights and histopathology of the organs will be determined.

D. Contractile behavior in vitro of umbilical arteries and their sensitivities to nicotine and prostoglandin will be determined.
(see attached)

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E. Placental enzymes (aryl hydrocarbon hydroxylase, cholesterol sidechain-splitting enzyme, and androgen aromatase activities will be quantitated in vitro.

F. Enzyme activities in fetal liver, adrenal gland, kidney, intestine and brain will be determined selectively (see below):

Organ	Enzyme Activity
Placenta (Pharmacology)	aryl hydrocarbon hydroxylase cholesterol sidechain-splitting enzyme androgen aromatization
Liver (Obstetrics and Pharmacology)	DHA 7α - hydroxylase 7β - hydroxylase 16α - hydroxylase 7 - hydroxysteroid dehydrogenase 16α - hydroxysteroid dehydrogenase 17β -hydroxysteroid dehydrogenase w-oxidation fatty acids aryl hydrocarbon hydroxylase azo dye N-demethylase
Adrenal (Pharmacology)	aryl hydrocarbon hydroxylase
Brain (Obstetrics)	progesterone 5α reductase progesterone 20α hydroxysteroid dehydrogenase
Intestine (Pharmacology)	glucuronyl transferase
Kidney (Pharmacology)	azo dye N-demethylase naphthylamine N-hydroxylase
Plasma (Pharmacology)	procaine esterase
Umbilical Cord (Obstetrics)	contractility studies with nicotine, prostaglandin, adrenergic and cholinergic stimulation

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8. Brief statement of working hypothesis:

The proposed program is based on the observation that cigarette smoking during human pregnancies is associated with reduced fetal birthweight at term gestation and produces profound changes in certain oxidative enzymes (aryl hydrocarbon hydroxylase, azo dye N-demethylase and cholesterol sidechain cleavage enzymes) of the placenta. The research involved will examine the hypothesis that the effects of cigarette smoking, and possibly marijuana smoking can produce different effects on these and on several other enzymic activities, and on fetal weight that are already recognizable in previable pregnancies. Any changes in the cardiopulmonary and metabolic-endocrine adjustments of the pregnant female, as they may alter fetal oxygenation via decreasing oxygen saturation or carbon monoxide toxicity, or via nicotine-related decreases in fetal perfusion, may be related to fetal growth and the altered enzyme activities. Those chosen for study are principally mixed function-oxidases utilizing cytochrome P-450 as the terminal oxidase, which requires molecular oxygen for its transformations, and that can be inhibited in vitro by small amounts of carbon monoxide.

9. Details of experimental design and procedures (append extra pages as necessary)

Clinical Subjects

Three groups of women in the first trimester (14-16 weeks) of pregnancy will be solicited for the studies, for which review and approval of the Biomedical Review Committee of the University of Washington will be obtained. Group one, nonsmokers; Group two, women smoking 20-30 cigarettes daily for the duration of the pregnancy; Group three, women regularly smoking marijuana for the duration of the pregnancy. If possible, the cardiovascular studies and blood sampling for metabolic endocrine assessments will be completed on outpatients (Clinical Research Center, approval pending). Abortions will be carried out vaginally after cervical dilatation with laminaria tents, followed by oxytocin infusion and extraction of the fetus, or with the stimulation of uterine contractions by the introduction of an extraovular catheter and infusion of oxytocic substances, followed by expulsion and/or extraction, as clinical management compatible with reasonable fetal tissue integrity necessitates.

Cardiopulmonary Studies

See Wong, et al., Anesthesiology, Vol. 38, p. 542, 1973 (reprints - Dr. Felix Freund) for methods of procedure.

Feto-Placental Morphology

The specimens will be picked up immediately after delivery and after clearance with the pathology department, and brought to the Central Laboratory of Human Embryology in the University Hospital. Fetal blood samples will be obtained as soon as possible. A complete autopsy will be performed, including crown-rump length, weight, crown-head length and the weight of organs. Organs weighed will be the brain, lungs, heart, thymus, thyroid, liver, spleen, adrenal, kidney, placenta and gonad. These measurements will be compared to our own standards (see publication by Tanimura, et al., "Weight Standards for Organs from Early Human Fetuses," 1971). We have unpublished data on the size and weight of the placenta. The organs will be distributed to the investigators and if possible, to other investigators not involved

(see attached)

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Item 9. continued

in this project. Representative portions of the organs will be fixed, sectioned and stained for histologic examination.

Quantitation of Plasma Lipids and Hormones

The following list will be determined by the Department of Laboratory Medicine:

A. Total cholesterol assays

Method: spectrophotometric analysis

References:
1. Zlatlos A., Zak B. and Boyle A. J. Lab. & Clin. Med., Vol. 41, p. 486, 1953.
2. Zak B., Dickerman R.C., White E.G. and Cherney P.J.' Am. J. Clin. Pathology, Vol. 24, p. 1307, 1954.
3. Leffler H. Am. J. Clin. Pathology, Vol. 31, p. 310, 1959.

B. Phospholipid assays

Method: spectrophotometric analysis after perchoric acid digestion

References:
1. Zilversmit D.B. and Davis A.K. J. Lab. & Clin. Med., Vol. 35, p. 155, 1950.
2. Banttlet G.R. J. Biol. Chemistry, Vol. 234, p. 466, 1959.

C. Triglyceride assays

Method: fluorimetric analysis

References:
1. Noble R.P. and Campbell F.M. Clin. Chem., Vol. 16, p. 166, 1970.
2. Kessler G. and Lederer H. "Fluorimetric Measurement of Triglycerides," Automated Analytical Chemistry; Technicon Symposia (series). ed., L.T. Speggs. New York: Mediad, Inc., p. 341, 1965.

D. Progesterone assays

Method: competitive protein binding

References:
1. Niell J.D., Johansson E.D., Datta J.K. and Knobil E. J. Clin. Endocr., Vol. 27, p. 1167, 1967.
2. Stone S., Nakamura R.M., Mishell D.R., Jr. and Thorney-croft I.H. Steroids, Vol. 17, p. 411, 1971.
3. Schiller H., Conrad S., Mahler E., Cox D. and Heinrichs W.L. (in preparation)

E. Estradiol assays

Method: radioimmunoassay analysis

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References: 1. Abraham G.E. J. Clin. Endocr., Vol. 29, p. 866, 1969.
2. Abraham G.E. Biochem. Med., Vol. 3, p. 365, 1970.

F. Carboxyhemoglobin assays

Method: spectrophotometric

Reference: 1. Maas A.H J., Hamelink M.L. and DeLeeuw R.J.M. Clin. Chim. Acta, Vol. 29, p. 303, 1970.

G. Human Chorionic Somatomammotrophin (HCS) assays

Method: radioimmunoassay

Reference 1. Spellacy W.N., Carlson K.L. and Birk S.A. Am. J. Ob. Gyn., Vol. 96, p. 1164, 1966.

H. Human Chorionic Gonadotrophin (HCG) assays

Method: radioimmunoassay

Reference: 1. Paulsen C.A., Gordon D.L., Carpenter R.W., Gandy H.M. and Drucker W.D. Recent Prog. Horm. Res., Vol. 24, p. 321, 1968.

Physiological Studies In Vitro on Umbilical Cord

Human umbilical arteries will be obtained as soon as possible after delivery. Up to five segments will be removed from the sample and placed in chambers and connected to sensitive isometric tersion transducers. Initially a hypoxic gas mixture containing 8% O_2, 5% CO_2 and 87% N_2 will be bubbled into the chamber to induce a relaxation of the muscular segment (Bor I. and Buntheroth W.G. "In Vitro Response to Oxygen of Human Umbilical Arteries and of Animal Ductus Arteriosus," Canadian J. Physiol. & Pharm., Vol. 48, pp. 500-502, 1970.). After a period of relaxation (approximately one to two hours) a hyperoxic gas mixture of 95% O_2 will be introduced for a period of 30 minutes. This technique usually induces a contraction in the arterial segments. Gas mixtures may be altered several times to insure a series of contractions and relaxations.

After an initial contraction-relaxation cycle, various amounts of nicotine or prostaglandins (the exact amounts to be determined by experimentation) will be added to the bath and an additional contraction-relaxation cycle produced. The various levels in sensitivity in the groups of umbilical artery segments will be noted then and compared. It will be feasible by this method to run an entire dose-response curve for a particular patient by using a multiple bath arrangement.

Fetoplacental Enzymology (Pharmacology)

Aryl hydrocarbon hydroxylase activities will be assayed by measuring the appearance of the fluorescent hydroxylated metabolites according to modifications of the method of

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Wattenberg, et al. (1962) as described by Juchau (1971). Cholesterol sidechain-cleavage will be determined by a modification of the methods of Morrison, et al. (1965) as described by Juchau, et al. (1972). The assay method for androgen aromatization utilizes liquid scintillation spectrometry, and will be performed by modifications (Juchau, et al. 1972) of the methods described by Shaw and Dalziel (1969). Azo dye N-demethylase activities will be studied utilizing the method described by Welch, et al. (1968). The w-oxidation of laurate will be assayed according to the method of Kusunose, et al. (1964). Glucuronyl transferase will be assayed according to methods described by Dutton (1963). Naphthylamine N-hydroxylase activities will be determined according to the methods described by Ziegler, et al. (1973) and procaine esterase will be assayed by the method of Kalow (1952).

Fetoplacental Enzymology (Obstetrics and Gynecology)

The dehydroepiandrosterone oxido-reductase activities of liver will be carried out according to procedures described by Tabei and Heinrichs (Endocrinol., Vol. 91, p. 967, 1972; Vol. 92, p. 1161, 1973; and Endocrinol., in press.). These procedures for quantitation of progesterone 5α reductase and 20α hydroxysteroid dehydrogenase activity in fetal brain utilize ^{14}C-4-progesterone and quantitation with liquid scintillation spectrometry. Data will be expressed as specific activity of enzymes, picamoles $hour^{-1} milligram^{-1}$. Protein will be determined by the Lowry procedure (Tabei T., Haga H., Heinrichs W.L. and Herrmann W.L. Submitted to Steroids, 1973).

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10. Space and facilities available (when elsewhere than item 2 indicates, state location):

The Pregnancy Termination Center of the Department of Obstetrics and Gynecology is directed by Dr. Louis Vontver at Harborview Medical Center, Seattle. It is staffed with obstetricians, anesthesiologists, nurses, and social workers active in terminating approximately 250 pregnancies annually. Physician staffing is contributed by clinical faculty working under the supervision of Dr. Vontver, who will coordinate the clinical management.

Cardiopulmonary studies will be performed in the Clinical Research Center of Harborview Medical Center under the direction of Dr. Felix Freund, member of the Anesthesia Research Center, University of Washington School of Medicine. Equipment described in the appended article by Wong, et al., Anesthesiology, Vol. 38, p. 542 (reprints - Dr. Felix Freund) will be utilized.

The Central Laboratory for Human Embryology is a completely equipped and fully staffed research laboratory of approximately 2,400 square feet in several rooms in the Child Development and Mental Retardation Center adjacent to the University Hospital. A portion of the time for professional staff for examination of the material is requested for this laboratory. Dissecting microscopes, instruments and several types of balances are available for this work. The laboratory is fully equipped for performing the histologic studies.

The Physiological Studies of Umbilical Cords will be carried out in the laboratories of Dr. John Conrad, Department of Obstetrics and Gynecology, University Hospital in facilities (see attached)

11. Additionall facilities required:

none

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12. Biographical sketches of investigator(s) and other professional personnel (append):

13. Publications: (five most recent and pertinent of investigator(s); append list, and provide reprints if available):

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Item 10. continued

The [illegible] Center of the Department of [illegible] is directed by Dr. Louis Vanvel at Harborview Medical Center, Seattle. It is shared with Obstetrics, including 625 square feet of working space, and containing two eight-channel recorders (one model HP 7700 and one Offner, type R) and one two-channel BLH recorder; five Sensitive Force Endevro 8107.2 transducers for small muscle studies; five Medium Force transducers; thermostatically regulated baths for up to eight test chambers; and one test station for sucrose gap potential measurement. The smaller microelectrode laboratory has 300 square feet for working space and contains two two-channel oscilloscopes (Tectronix 502); three negative capacitance preamplifiers; one four-channel pape recorder (Sanborn 150); one analog computer; one electronic stimulator (AEL 104A); time and signal generators; one oscilloscope camera (35 mm.); Leitz micromanipulators; Priar micromanipulators; Kopf microelectrode puller and dissection microscopes.

[illegible]

The Lipid and Hormone Assays will be carried out in the Cost Center of the Department of Laboratory Medicine, and in laboratories of the Department of Obstetrics and Gynecology by Dr. Harvey Schiller. A 600 square foot Endocrinology Laboratory, providing hormone assays for the University Hospital is located within the Department of Obstetrics and Gynecology and will be the site of these quantitative estimates. This laboratory and an adjacent instrument room are equipped with spectrophotometers, Barbara Coleman model 10 gas liquid chromatographs, Packard model 6240 Liquid Scintillation Spectrometers and strip scanners, water baths, evaporative extractors, ventilated hoods, etc.

Fetoplacental Enzymology (Pharmacology) will be completed in facilities comprising one biochemical pharmacology laboratory of approximately 600 square feet, with ready access to two other well equipped biochemical laboratories in the immediate vicinity. These include approximately 1,700 square feet; 330 square feet of additional laboratory space also has been acquired recently. A cold room with facilities for enzyme isolation and tissue preparation (immediately adjacent) will also be available.

The major pertinent items of equipment available for the proposed research project include:

1. Spinco Model L ultracentrifuge
2. Beckman DU spectrophotometer
3. Gilford Model 2000 recording spectrophotometer with constant temperature and automatic sample changer attachments and recorder
4. Beckman Expandomatic pH meter
5. Beckman DB spectrophotometer
6. Liquid scintillation counter - Nuclear Chicago, Mark I
7. Buchler Flash evaporator
8. Three Dubnoff shaking incubators; one Burrel shaking machine; assorted water baths and centrifuges
9. Constant temperature, explosion-proof thin layer chromatography oven
10. Mettler Precision balance; Mettler top-loader balance
11. Automatic glassware washer

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Fetoplacental Enzymology (Obstetrics and Gynecology). A Biochemical Endocrinology Laboratory in the Department of Obstetrics and Gynecology comprises 400 square feet of working space, including a hood, Barbara Coleman gas liquid chromatograph, evaporative extractors and temperature-related water bath where Dr. Toru Tabei will carry out assays. He will have the use of the liquid scintillation spectrometers in the adjacent instrument room of the department. In addition, an 80-foot-square cold room with a Spiuco L-2 preparative ultra centrifuge is available for his use.

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14. First year budget:

A. Salaries (give names or state "to be recruited")
Professional (give % time of investigator(s) even if no salary requested)

	Position	% time	Benefits	Amount
W. LeRoy Heinrichs	(Principle Investig.)	10		$
Toru Tabei	Res. Ass't. Prof. (Ob/GYN)	50		REDACTED
Pearl Namkung	Res. Tech. II (Ob/GYN)	100		
To be recruited	Res. Tech. I (Pharmacol.)	100		
To be recruited	Secretary (Ob/GYN)	50		REDACTED
Alan Fantel	Ass't. Teratologist (Peds.)	50		
John Conrad (Ob/GYN)	Co Investigator	10		REDACTED
Mont Juchau (Pharmacology)	"	15		
Felix Freund (Anesthesiology)	"	10		
Harvey Schiller (Ob/GYN)	"	10		
Thomas Shepard (Pediatrics)	"	5		

Sub-Total for A REDACTED

B. Consumable supplies (by major categories)

Obstetrics and Gynecology		
	Toru Tabei	3,000
	John Conrad	1,000
Pharmacology		
	Mont Juchau	3,000
	Sub-Total for B	7,000

C. Other expenses (itemize)

Publication costs	750
Equipment	600
Laboratory Medicine (plasma, lipids, hormones)	4,000
Patient Costs (30 patients at $100 each)	3,000
Travel (3 cross country trips)	1,800
Sub-Total for C	10,150

Running Total of A + B + C REDACTED

D Permanent equipment (itemize)

Sub-Total for D

E. Indirect costs (15% of A+B+C) (minus equipment) E 9,458

Total request REDACTED

15. Estimated future requirements.

	Salaries	Consumable Suppl.	Other Expenses	Permanent Equip	Indirect Costs	Total
Year 2						
Year 3						

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16. Other sources of financial support: (for M.R. Juchau, Ph.D.)
List financial support from all sources, including own institution, for this and related research projects.

CURRENTLY ACTIVE

Title of Project	Source (give grant numbers)	Amount	Inclusive Dates
Biotransformation of Drug Substrates in Human Fetal Tissues	National Foundation CRBS 250	15,975	July 1, 1973 - June 30, 1974
Metabolism of Drug Substrates by Human Placenta	NIH - HD 04839	24,980	January 1, 1973 - December 31, 1973

PENDING OR PLANNED

Title of Project	Source (give grant numbers)	Amount	Inclusive Dates

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It is understood that the investigator and institutional officers in applying for a grant have read and accept the Councills "Statement of Policy Containing Conditions and Terms Under Which Project Grants Are Made."

Principal investigator

Typed Name W. LeRoy Heinrichs, M.D., Ph.D.

Signature [signature] Date 7-23-73

Telephone (206) 543-3580
Area Code Number Extension

Checks payable to

Donald R. Baldwin, Director
Office of Grants and Contract Services

Mailing address for checks

211 Administration Bldg. AG-50
University of Washington
Seattle WA 98195

Responsible officer of institution

[signature]
George W. Farwell, Ph.D.
Vice President for Research

Telephone (206) 543-0151
Area Code Number Extension

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CURRICULUM VITAE

William LeRoy Heinrichs

Personal Data:

Birth Date
Birth Place
Citizenship
Marital Status
Children

REDACTED REDACTED

Education:

High School	Central High School Collinsville, Oklahoma	1946-50
College: B.S.	Southwestern State College Weatherford, Oklahoma	1951-54
Medical School: M.D.	University of Oklahoma School of Medicine Oklahoma City, Oklahoma	1954-58
Rotating Intern	St. Anthony Hospital (Affiliate of University of Oklahoma Medical School) Oklahoma City, Oklahoma	1958-59
Ob-Gyn Resident	Harper Hospital (Affiliate of Wayne State University Medical School) Detroit, Michigan	1959-62
PHS Post-Residency Training Program: M. Sci. and Ph.D. - Biochemistry	Department of Obstetrics & Gynecology University of Oregon Medical School Portland, Oregon	1962-67

Academic Honors:

High School	Valedictorian of the graduating class	1950
College	Elected Alpha Phi Sigma and Beta Beta Beta (National Honor Fraternities)	1953

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Academic Honors (Cont'd):

Medical School	Student Research Achievement Award in Biochemistry	1958
Ob-Gyn Residency	Second Award for a Scientific Paper	1962
Post-Residency Training	Appointed Macy Fellow in Obstetrics and Reproduction	1966
Career	Presidents First Award for Research, American College of Obstetricians and Gynecologists	1970

Academic Appointments:

Clinical Instructor	Department of Obstetrics & Gynecology University of Oregon Medical School Portland, Oregon	1965-67
Assistant Professor	Department of Obstetrics and Gynecology University of Washington School of Medicine Seattle, Washington	1967-69
Associate Professor	Department of Obstetrics and Gynecology University of Washington School of Medicine Seattle, Washington	1969-72
Professor	Department of Obstetrics and Gynecology University of Washington School of Medicine Seattle, Washington	1972-

Hospital Appointments:

Attending Staff	Good Samaritan Hospital Portland, Oregon	1965-67
Attending Staff	University Hospital, and Harborview Medical Center, Seattle, Washington	1967-
Consultant	U.S. Public Health Service Hospital Seattle, Washington	1971-
Consultant	Madigan General Hospital Tacoma, Washington	1971-

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Professional Organizations:

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Participation in Symposia or International Scientific Conferences:

Ghent, Belgium	2nd Symposium on Steroid Hormones: "Androgens in Normal and Pathological Conditions."	1965
Princeton, New Jersey	Macy Conference on Research and Education in Obstetrics and Reproduction.	1967
Rome, Italy	4th Meeting of the International Study Group for Steroid Hormones.	1969

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Organization Responsibilities:

Program Committee Member	Washington State Obstetrical Association	1969-

School of Medicine Committees:

Subject Committee	Embryology and Tissues Structures	1968-69
Advisory Committee	E-1970 Medical Students	1970-

University Hospital Committees:

Member	Infection Committee	1968-70
Member	Internship Interviewing	1969-70
Member	Perinatal Mortality	1968-69
Member	Scientific Advisory Board Clinical Research Center	1969-

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BIBLIOGRAPHY

William LeRoy Heinrichs, M.D., Ph.D.

1. Heinrichs, W.L.: Studies of serum proteins and glycoproteins in monozygotic (MZ) and dizygotic (DZ) twins. Thesis submitted to the Student Research Achievement Committee, University of Oklahoma School of Medicine, 1958.

2. Heinrichs, W.L. and M.R. Shetlar: Serum glycoproteins in monozygotic and dizygotic twins. Proc. Soc. Exp. Biol. & Med. 99: 132, 1958.

3. Heinrichs, W.L.: Soft tissue dystocia. Harper Hosp. Bull. 19: 80, 1961.

4. Heinrichs, W.L., Climie, A.R.W. and Cook, J.C.: Cure of primary mesodermal mixed tumor by radiotherapy. Obstet. & Gynec. 19: 537, 1962.

5. Heinrichs, W.L., Kommesser, J.G. and Tullock, J.A.: Continuous lumbar epidural anesthesia in obstetrics. Harper Hosp. Bull. 20: 6, 1962.

6. Heinrichs, W.L.: The neutrophile alkaline phosphatase test in pregnancy. Harper Hosp. Bull. 20: 107, 1962.

7. Heinrichs, W.L.: Pelvic hematomas following delivery. Harper Hosp. Bull. 21: 56, 1963.

8. Climie, A.R.W., Heinrichs, W.L., and I.J. Foster: Neutrophilic alkaline phosphatase test: A review with emphasis on findings in pregnancy. Tech. Bull. Regis. Med. Tech. 32: 95, 1962.

9. Colás, A., Heinrichs, W.L., and Tatum, H.J.: Pettenkofer chromogens in the maternal and fetal circulations: detections of 3ß, 16a-dihydroxyandrost-5-en-17-one in umbilical cord blood. Steroids 3: 417, 1964.

10. Colás, A., and Heinrichs, W.L.: Pettenkofer chromogens in maternal and fetal circulations: anencephalic pregnancies, cesarean sections and tentative identification of 3ß, 17ß-dihydroxyandrost-5-en-16-one in umbilical cord blood. Steroids 5: 753, 1965.

11. Heinrichs, W.L.: A method for the analysis of specific urinary 3ß-hydroxy-Δ^5-steroids and some applications in clinical medicine. Thesis presented for the Master of Science Degree in Biochemistry, University of Oregon Medical School, 1965.

12. Heinrichs, W.L., Feder, H.H., and Colás, A.: The steroid 16a-hydroxylase system in mammalian liver. Steroids 7: 91, 1966.

13. Heinrichs, W.L., Mushen, R.L., and Colás, A.: The 7ß-hydroxylation of 3ß-hydroxyandrost-5-en-17-one by hepatic microsomes. Steroids 9: 23, 1967.

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14. Heinrichs, W.L.: Hydroxylations of dehydroepiandrosterone by microsomal fractions from mammalian liver. Thesis presented to the Department of Biochemistry and the Graduate Division of the University of Oregon Medical School, in partial fulfillment of the requirements for the degree of Doctor of Philosophy, 1967.

15. Heinrichs, W.L., and Colas, A.: The selective stimulation, inhibition and physico-chemical alteration of the 7- and 16α-hydroxylases of 3ß-hydroxy-androst-5-en-17-one and drug-metabolizing enzymes. Biochemistry 7:2273, 1968.

16. Herrmann, W.L., Spadoni, L.R., and Heinrichs, W.L.: "Androgens and the Gynecologist", chapter in The Adrenal (N.P. Christy, ed.) In press.

17. Wyss, R.H., Heinrichs, W.L., and Herrmann, W.L.: Some species differences of uterine estradiol receptors. J. Clin. Endocrinol. & Metab. 28: 1227, 1968.

18. Wyss, R.H., Karsznia, R., Heinrichs, W.L., and Herrmann, W.L.: Inhibition of uterine receptor binding of estradiol by anti-estrogens (clomiphene and CL-868). J. Clin. Endocrinol. & Metab. 28: 1824, 1968.

19. Karsznia, R., Wyss, R., Heinrichs, W.L., and Herrmann, W.L.: Testicular feminization: an apparent enzyme defect. Gynaecologia. 167: 177, 1969.

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21. Kahwanago, I., Heinrichs, W.L., and Herrmann, W.L.: Isolation of estradiol 'receptors' from bovine hypothalamus and pituitary gland. Nature 223: 313, 1969.

22. Heinrichs, W.L., and Colas, A.: Hepatic microsomal 16α-hydroxylation of 3ß-hydroxyandrost-5-en-17-one (DHA) by fetal, newborn and adult Rhesus monkeys. Gen. and Comp. Endo. 14:159, 1970.

23. Kahwanago, I., Heinrichs, W.L., and Herrmann, W.L.: Estradiol 'receptors' in the pituitary gland and hypothalamus. Endocrinology 86: 1319, 1970.

24. Heinrichs, W.L., Dillingham, L.L.: Bornean orang twins born in captivity. Folia Primatol. 13: 150, 1970.

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26. Heinrichs, W.L., Gellert, R.J., Bakke, J.L., and Lawrence, N.: DDT administered to neonatal rats induces persistent estrus syndrome. Science, 173: 642, 1971.

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Source: https://www.industrydocuments.ucsf.edu/docs/lrvm0000

27. Heinrichs, W.L., and Ueland, K.: Fetal Management. Chapter, in Practice in Pediatrics (Brenneman-Kelley, eds.) Harper & Row, 1972.

28. Farber, M., Conrad, S.H., Heinrichs, W.L., and Herrmann, W.L.: Estradiol binding by fibroid tumors and normal myometrium. Obstet. Gynec. 40: 479, 1972.

29. Gellert, R.J., Heinrichs, W.L., and Swerdloff, R.S.: DDT homologues: estrogen like effects on the vagina, uterus, and pituitary of the rat. Endocrinology 91: 1095, 1972.

30. Tabei, T., and Heinrichs, W.L.: Enzymatic oxidation and reduction of C_{19}-Δ^5-3ß-hydroxysteroids by hepatic microsomes. I. Biosynthesis of 3ß, 17ß-dihydroxy-androst-5-16-one and sex differences in adult rats. Endocrinology 91: 969, 1972.

31. Tabei, T., and Heinrichs, W.L.: Enzymatic oxidation and reduction of C_{19}-Δ^5-3ß-hydroxysteroids by hepatic microsomes. II. Effect of Age in Rats on 16, 17-oxido-reduction of 3ß-hydroxyandrost-5-en-17-one (DHA). Endocrinology 92: 1161, 1973.

32. Omenn, G.S., Figley, M.M., Graham, C.B., and Heinrichs, W.L.: Prospects for radiographic intrauterine diagnosis: The syndrome of thrombocytopenia with absent radii (TAR). New Eng. J. Med. April, 1973.

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ABSTRACTS

1. Colas, A., Heinrichs, W.L., and Tatum, H.J.: The metabolism of 3ß, 16a-dihydroxyandrost-5-en-17-one by human placenta. 6th Inter. Cong. of Biochem. 32: 569, 1964.

2. Heinrichs, W.L., and Colas, A.: Quantitation of urinary dehydroepiandrosterone 16a-hydroxydehydroepiandrosterone and other 3ß-hydroxy-Δ^5-steroids in pregnancy and hirsutism. Androgens in Normal and Pathological Conditions. Proc. 2nd Symp. on Steroid Hormones. June, 1965, Ghent, Belgium.; p. 62, Excerpta Medica Foundation, New York, 1966.

3. Heinrichs, W.L., and Colas, A.: Hepatic microsomal hydroxylations of dehydroepiandrosterone (DHA). 49th Meeting of The Endocrine Society, 211: 134, 1967.

4. Heinrichs, W.L., Karsznia, R., Wyss, R., and Herrmann, W.L.: Testicular feminization: an apparent enzyme defect. Clin. Res. 17: 143, 1969.

5. Heinrichs, W.L., Kahwanago, I., and Herrmann, W.L.: Binding of ^{3}H-estradiol by 'receptors' in bovine hypothalamus and pituitary gland, and inhibition by clomiphene citrate. 16th Annual Meeting of the Society for Gynecologic Investigation, Denver, Colo., 1969.

6. Farber, M., Conrad, S., Heinrichs, W.L., and Herrmann, W.L.: Binding of estradiol by normal and neoplastic human myometrium. The 51st Annual Meeting of The Endocrine Society, New York, 164: 112, 1969.

7. Depp, R., Pion, R.J., and Heinrichs, W.L.: Inhibition of pregnenolone 3ß-hydroxy-steroid dehydrogenase system in human placenta and corpus luteum of pregnancy. The 51st Annual Meeting of The Endocrine Society, New York, 211: 136, 1969.

8. Kahwanago, I., Heinrichs, W.L., and Herrmann, W.L.: Species and age differences in estradiol 'receptors'. The District VIII Annual Meeting of the American College of Obstetricians and Gynecologists, Albuquerque, New Mexico, 1969.

9. Youatt, G., Wyss, H.I., Heinrichs, W.L., and Herrmann, W.L.: Binding of pregnenolone in cytoplasm from rat and dog prostate. The 52nd Annual Meeting of The Endocrine Society, St. Louis, 1970.

10. Wyss, H.I., Youatt, G., Heinrichs, W.L., and Herrmann, W.L.: Influence of magnesium on the stability of the estradiol 'receptor' in uterine cytoplasm. The 52nd Annual Meeting of The Endocrine Society, St. Louis, 1970.

11. Heinrichs, W.L.: Oxidative metabolism of steroids and drugs by hepatic microsomes from pregnant rats. Presented at the 17th Annual Meeting of the Society for Gynecologic Investigation, New Orleans, 1970.

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Abstracts (Cont'd):

12. Tabei, T., and Heinrichs, W.L.: Puberty and hepatic 16-oxygenation of 3ß-hydroxyandrost-5-en-17-one (DHA). The 53rd Annual Meeting of The Endocrine Society, San Francisco, 1971.

13. Heinrichs, W.L., Haga, H., and Tabei, T.: Progesterone 5α-reductase activity in cell-free homogenates of rat brain and other tissues. The 19th Annual Meeting of The Society for Gynecologic Investigation, San Francisco, 1972, No.75.

14. Omenn, G.S., Figley, M.M., and Heinrichs, W.L.: Radiographic intrauterine diagnosis for the TAR syndrome (thrombocytopenia with absent radii). Presented at the Annual Meeting, American Society of Human Genetics, Philadelphia, 1972. Am. J. Hum. Genet. 24: 31a, 1972.

15. Tabei, T., Haga, H., Heinrichs, W.L., and Herrmann, W.L.: Metabolism of progesterone by the brain and the pituitary gland. Clin. Res. 21: 206, 1973.

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IN PRESS

1. Heinrichs, W.L.: Steroid hydroxylases and drug-metabolizing enzymes in hepatic microsomes. I. Pregnancy and administration of phenobarbital or etiocholanolone. Submitted and being revised for Archiv. Biochem. Biophys., 1973.

2. Tabei, T., and Heinrichs, W.L.: Enzymatic oxidation and reduction of C_{19}-Δ^5-3ß-hydroxysteroids by hepatic microsomes. III. 7-oxygenation of 3ß-hydroxyandrost-5-en-17-one (DHA) during puberty in rats. Submitted to Endocrinology, 1973.

3. Tabei, T., and Heinrichs, W.L.: Enzymatic oxidation and reduction of C_{19}-Δ^5-3ß-hydroxysteroids by hepatic microsomes. IV. Critical period for the neonatal differentiation of certain mixed-function oxidases. Submitted to Endocrinology, 1973.

IN PREPARATION

1. Haga, H., Tabei, T., and Heinrichs, W.L.: Progesterone 5α-reductase activity in cell-free homogenates of rat brain and other tissues.

2. Tabei, T., and Heinrichs, W.L.: Progesterone 5α- and 20α-reduction by rat brain and pituitary gland.

3. Forster, M.S., and Heinrichs, W.L.: In vitro binding of DDT and its homologues to estrogen receptors in target tissues of rats.

4. Forster, M.S., and Heinrichs, W.L.: Estrogen receptor binding capacity in hyperplastic and neoplastic human endometrium.

5. Forster, M.S., Wyss, H., Gellert, R.J., and Heinrichs, W.L.: Changes in estrogen receptor in target tissues after neonatal estrogen induced constant estrus.

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R: REDACTED MATERIAL

Council for Tob. Research

CURRICULUM VITAE

Toru Tabei, M.D., Ph.D.

Personal Data:

Birth Date	REDACTED
Birth Place	
Citizenship	
Marital Status	
Children	REDACTED

Education:

High School	Kumagaya High School, Japan	1951-54
B.S.	Chiba Governmental College Chiba, Japan	1954-57
M.D.	University of Chiba School of Medicine Chiba, Japan	
Rotating Intern	Toranomon Hospital Tokyo, Japan	1961-62
Resident; and Post-residency training program (Ph.D.)	Department of Obstetrics & Gynecology University of Tokyo Tokyo, Japan	1962-66
Senior Fellow	Department of Obstetrics & Gynecology University of Washington School of Medicine Seattle, Washington	1970-71

Academic Appointments:

Research Associate	Montefiore Hospital Department of Medicine University of Pittsburgh Pittsburgh, Pennsylvania	1966-68

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Academic Appointments (Cont'd):

Assistant Professor	Department of Obstetrics & Gynecology University of Tokyo Tokyo, Japan	1969-70
Research Assistant Professor	Department of Obstetrics & Gynecology University of Washington School of Medicine Seattle, Washington	1971-

Hospital Appointments:

Clinical Attending Staff	Department of Obstetrics & Gynecology University Hospital University of Tokyo Tokyo, Japan	1968-70
Clinical Attending Staff	Sanraku Hospital (Affiliate of the University of Tokyo Tokyo, Japan	1968-70

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BIBLIOGRAPHY

Toru Tabei, M.D., Ph.D.

1. Nakayama, T., Arai, K., Satoh, K., Nagatomi, K., Tabei, T., and Yanaihara, T.: The formation of estriol from estradiol-17ß by the human fetal adrenal tissue. Endocrinologia Japonica 13: 153, 1966.

2. Nakayama, T., Arai, K., Yanaihara, T., Tabei, T., Satoh, K., and Nagatomi, K.: Oestrogen metabolism in anencephalus. Acta Endocrinologica 55: 369, 1967.

3. Nakayama, T., Arai, K., Tabei, T., Yanaihara, T., Satoh, K., and Nagatomi, K.: Biosynthesis of estrogens in in vitro perfusion of the human placenta. Endocrinologia Japonica 14: 251, 1967.

4. Nakayama, T., Arai, K., Nagatomi, K., Satoh, K., Tabei, T., Yanaihara, T., and Fujita, Y.: Biosynthesis of estrogens by the perfused human ovary. I. Conversion of progesterone-^{14}C and androst-4-ene-3, 17-dione-^{14}C to estradiol-17ß. Endocrinologia Japonica 14: 259, 1967.

5. Nakayama, T., Arai, K., Yanaihara, T., Satoh, K., Nagatomi, K., Tabei T., and Fujita, Y.: Formation of estrogens in the feto-placental compartments. Endocrinologia Japonica 15: 135, 1968.

6. Tabei, T.: Biosynthesis of estrogens in the human placenta. (Thesis presented to the Department of Obstetrics and Gynecology, University of Tokyo). Acta Obstetrica et Gynaecologica Japonica 17: 1, 1970.

7. Tabei, T., and Heinrichs, W.L.:, Enzymatic oxidation and reduction of C_{19}-Δ^5-3ß-hydroxysteroids by hepatic microsomes. I.. Biosynthesis of 3ß, 17ß-dihydroxyandrost-5-16-one and sex differences in adult rats. Endocrinology 91: 969, 1972.

8. Tabei, T., and Heinrichs, W.L.: Enzymatic oxidation and reduction of C_{19}-Δ^5-3ß-hydroxysteroids by hepatic microsomes. II. Effect of age in rats on 16, 17-oxido-reduction of 3ß-hydroxyandrost-5-en-17-one (DHA). Endocrinology 92: 1161, 1973.

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ABSTRACTS

1. Tabei, T., and Troen, P.: Studies of C-6 hydroxylation of C_{21} steroids in human placenta. J. Clin. Invest. 48: 82a, 1969. (Presented at the 61st Annual Meeting of the American Society for Clinical Investigation, Atlantic City, 1969).

2. Tabei, T., and Heinrichs, W.L.: Puberty and hepatic 16-oxygenation of 3ß-hydroxyandrost-5-en-17-one (DHA). The 53rd Annual Meeting of The Endocrine Society, San Francisco, 1971.

3. Heinrichs, W.L., Haga, H., and Tabei, T.: Progesterone 5α-reductase activity in cell-free homogenates of rat brain and other tissues. The 19th Annual Meeting of The Society for Gynecologic Investigation, San Francisco, 1972, No. 75.

4. Tabei, T., Haga, H., and Heinrichs, W.L., and Herrmann, W.L.: Metabolism of progesterone by the brain and the pituitary gland. Clin. Res. 21: 206, 1973.

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IN PRESS AND IN PREPARATION

1. Tabei, T., and Heinrichs, W.L.: Enzymatic oxidation and reduction of C_{19}-Δ^5-3ß-hydroxysteroids by hepatic microsomes. III. 7-oxygenation of 3ß-hydroxyandrost-5-en-17-one (DHA) during puberty in rats. Submitted to Endocrinology, 1973.

2. Tabei, T., and Heinrichs, W.L.: Enzymatic oxidation and reduction of C_{19}-Δ^5-3ß-hydroxysteroids by hepatic microsomes. IV. Critical period for the neonatal differentiation of certain mixed-function oxidases. Submitted to Endocrinology, 1973.

3. Haga, H., Tabei, T., and Heinrichs, W.L.: Progesterone 5α-reductase activity in cell-free homogenates of rat brain and other tissues. In preparation, 1973.

4. Tabei, T., and Heinrichs, W.L.: Progesterone 5α- and 20α-reduction by rat brain and pituitary gland. In preparation, 1973.

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TORU TABEI, M.D.

See publications for Heinrichs, W.L. for reprints for both Investigators.

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CURRICULUM VITAE

John T. Conrad, Ph.D.

Personal Data

Date of Birth
Place of Birth
Citizenship
Marital Status
Children

REDACTED

Education

B.A.	New York University Washington Square College New York, New York	1951
M.S.	New York University New York, New York	1955
Ph.D.	New York University New York, New York	1961

Academic Appointments

Research Assistant	Department of Biology Washington Square College New York University New York, New York	1952-53
Research Assistant	Sloan-Kettering Institute for Cancer Research	1953-54
Teaching Fellow	Department of Biology Washington Square College New York University New York, New York	1955-57
Research Assistant	Department of Internal Medicine Neurology Section Yale University School of Medicine New Haven, Connecticut	1957-60
Instructor	Department of Physiology Yale University School of Medicine New Haven, Connecticut	1960-62

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R: REDACTED MATERIAL

Assistant Professor	Department of Physiology and Biophysics University of Washington School of Medicine Seattle, Washington	1962-67
Associate Professor	Departments of Physiology and Biophysics and Obstetrics and Gynecology University of Washington School of Medicine Seattle, Washington	1967-Present

Honors

New York State War Service Scholarship, 1951-55
New York University Scholar, 1961
Visiting Biologist under AIBS/OBE, 1967-71

Lalor Foundation Fellow 1968-69

Professional Societies

REDACTED REDACTED

Committees

Communications Subcommittee, Medical Illustration and Photography, 1969-70

Perinatal Biology Committee of the Child Development and Mental Retardation Center, 1969-Present (Chairman, 1973)

Comparative Physiology Training Committee, 1970-Present

Library Advisory Committee, 1972-73

Citizens Advisory Committee for Sunset Community School, Shoreline School District, 1973

Vestryman and Senior Warden, St. Dunstans Episcopal Church, Seattle, Washington, 1973

Referee Editor

American Journal of Ob/Gyn
Gynecologic Investigation
Life Sciences
American Journal of Physiology

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BIBLIOGRAPHY

John T. Conrad, Ph.D.

1. Bane, H.N., Conrad, J.T., and Tarnowski, G.S.: Combination Therapy of Malignant Tumors with Ionizing Radiations and Chemicals. Cancer Research 17:551-566, 1957.

2. Tarnowski, G.S., Bane, H.N., Conrad, J.T., Nickson, J.J., Stock, G.C., and Sugiura, K.: Effects of Combinations of Radiation and Chemotherapeutic Agents against Experimental Animal Tumors. Cancer Research Screening Data 1, 18:225-245, 1958.

3. Conrad, J.T. and Glaser, G.H.: A Study of Membrane Resting and Action Potentials of Dystrophic Mammalian Muscle. Trans. Amer. Neurol. Assoc. 84th Annual Meeting (1959). The William Byrd Press, Inc., Richmond, Virginia.

4. Conrad, J.T. and Glaser, G.H.: Electrical Activity of Mammalian Skeletal Muscle Studied by Microelectrodes. Effects of Electrolyte Alterations. Chapter 4, Myasthenia Gravis, edited by Henry R. Viets. Charles C. Thomas, Springfield, Illinois, 1960.

5. Chu, F.C., Conrad, J.T., Bane, H.N., Glickman, A.S., and Nickson, J.J.: Quantitative and Qualitative Evaluation of Skin Erythema. 1. Technique of Measurement and Description of the Reaction. Radiology 75:406-410, 1960.

6. Conrad, J.T. and Glaser, G.H.: Bioelectric Properties of Dystrophic Mammalian Muscle. Archives of Neurology 5:46-59, 1961.

7. Conrad, J.T.: The Veratrine Response in Frog Muscle as Studied by Intracellular Electrodes. Dissertation Abstracts xxii: 2:612-613, 1961.

8. Conrad, J.T. and Glaser, G.H.: Neuromuscular Fatigue in Dystrophic Muscle. Nature 196, 4858, 997-998, 1962.

9. Conrad, J.T. and Glaser, G.H.: Spontaneous Activity at Myoneural Junction in Dystrophic Muscle. Arch. Neurology 11:310-316, 1964.

10. Conrad, J.T., Kuhn, W.K., and Johnson, W.L.: Stress Relaxation in Human Uterine Muscle. (Abstract). Obst. & Gynec. 25:419, 1965.

11. Johnson, W.L., Conrad, J.T., Whitney, D., and Graybeal, N.: The Effect of Pregnancy and Enovid on Length-tension Relationships in the Rabbit Aorta. Am. J. Obst. & Gynec. 93:179, 1965.

12. Woodbury, W., Gordon, A.M., and Conrad, J.T.: "Muscle" in Physiology and Biophysics. Edited by T.C. Ruch and Harry D. Patton. W.B. Saunders Co., Philadelphia and London, 1965.

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13. Conrad, J.T., Kuhn, W.K., and Johnson, W.L.: Stress Relaxation in Human Uterine Muscle. Am. J. Obstet. & Gynec. 95:254-265, 1966.

14. Conrad, J.T., Kuhn, W.K., Johnson, W.L., and Hunter, C.A., Jr.: Passive Stretch Relationships in Human Uterine Muscle. Am. J. Obstet. & Gynec. 96:1055-1059, 1966.

15. Conrad, J.T. and Kuhn, W.K.: The Active Length-tension Relationship in Human Uterine Muscle. Am. J. Obstet. & Gynec. 97:154-160, 1967.

16. Mossman, R. and Conrad, J.T.: The In Vitro Blocking Effect and Oxytocic Effect of the Water-Soluble Estrogens on Pregnant Human, Mouse and Rat Uteri. Amer. J. Obstet. & Gynec. 99:539-545, 1967.

17. Tahmoush, Albert, Conrad, J.T., Abrams, R., and Long, E.: The Conduction Velocity of the Action Potential in the In Vitro Rat Uterus as Modified by Estrogens and Pregnancy. (Abstract). Proceedings of the International Union of Physiological Sciences VII: 426, 1968.

18. Conrad, J.T., Aoba, H., and Shimizu, T.: The Effect of Estrogenic and Progestational Steroids Upon the Transmembrane Potentials of Cells from the Frog Muscle. Federation Proceedings 28:771, 1969.

19. Dawson, J.E. and Conrad, J.T.: The Effect of Human Chorionic Gonadotropin (HCG) and Luteinizing Hormone (LH) upon the Membrane Potential of Unovulated Frog Oocytes. The Physiologist 12:106, 1969.

20. Mossman, R., and Conrad, J.T.: Oxytocic and Modulating Effects of Water-Soluble Hydrocortisone and Methylprednisolone upon In Vitro Contractions of Myometrium. Am. J. Obstet. & Gynec. 105:897, 1969.

21. Conrad, J.T.: The Biophysics of Nidation. The Biology of the Blastocyst. Edited by R.J. Blandau. The University of Chicago Press, 1971.

22. Conrad, J.T.: Obstetrics Chapter in Medical Engineering: Projections for the Future. Edited by R. Rushner. Academic Press, New York, Spring, 1972.

23. Dawson, J.E. and J.T. Conrad: "The Effect of Human Chorionic Gonadotropin and Luteinizing Hormone upon the Membrane Potential of Unovulated Frog Oocytes. Biology of Reproduction 6:58-66, 1972.

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MANUSCRIPTS IN PRESS

John T. Conrad, Ph.D.

1. Conrad, J.T. and Onwudiwe, F.: The effects of the prostaglandins, PGE and $PGF_{2\alpha}$ upon the in vitro isthmug, ampulla and uterus of the estrus rabbit. Prostaglandins (July, 1973).

2. Conrad, J.T.: "Uterine biomechanics" in Biomechanics, ed., D.N. Ghista. Mosby Co., St. Louis, Mo.

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12. Biographical sketch: 27

BIOGRAPHICAL SKETCH

(Give the following information for all professional personnel listed on page 3, beginning with the Principal Investigator. Use continuation pages and follow the same general format for each person.)

NAME	TITLE	BIRTHDATE (Mo., Day, Yr.)
uchau, Mont R.	Associate Professor	REDACTED
PLACE OF BIRTH (City, State, Country)	**PRESENT NATIONALITY (If non U.S. citizen, indicate kind of visa and expiration date)**	**SEX**
REDACTED	REDACTED	REDACTED

EDUCATION *(Begin with baccalaureate training and include postdoctoral)*

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	SCIENTIFIC FIELD
Idaho State College--Pocatello, Idaho	B.S.	1960	Pharmacy
Washington State U.--Pullman, Wash.	M.S.	1963	Pharmacology
University of Iowa--Iowa City, Iowa	Ph.D.	1966	Pharmacology

HONORS

Who's Who in American Colleges and Universities--1960
Who's Who in the West--1973

MAJOR RESEARCH INTEREST	ROLE IN PROPOSED PROJECT
Developmental Biochemical Pharmacology	Principal Investigator

RESEARCH SUPPORT *(See instructions)*

Biotransformation of Drug Substrates in Human Fetal Tissues,
CRBS-2500
July 1, 1973-June 30, 1974--$13,832 (Total Project Period), 15% time.
National Foundation (March of Dimes).

RESEARCH AND/OR PROFESSIONAL EXPERIENCE *(Starting with present position, list training and experience relevant to area of project. List all or most representative publications. Do not exceed 3 pages for each individual.)*

Associate Professor of Pharmacology, School of Medicine, University of Washington(1973-preser
Assistant Professor of Pharmacology, School of Medicine, University of Washington (1969-73)
Assistant Professor of Biochemical Pharmacology, School of Pharmacy, State University of New York at Buffalo (1967-69)
Instructor in Biochemical Pharmacology, School of Pharmacy, State University of New York at Buffalo (1966-67).
U.S.P.H.S. Graduate Trainee, The University of Iowa (1963-66)
Research Assistant, Washington State University (1962-63)
Teaching Assistant, Washington State University (1961-62)
Registered Pharmacist, Idano, Nevada (1960-present)
Publications: See Section A, Number 15, Item d (pp. 20-21).

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13. Recent and pertinent publications (reprints attached):

1. M.R. Juchau, M.G. Pedersen and K.G. Symms: Hydroxylation of 3,4-benzpyrene in human fetal tissue homogenates. Biochem. Pharmacol. 21: 2269, 1972.

2. K.G. Symms and M.R. Juchau: Mechanism of aromatic nitro group reduction in the soluble fraction of human placenta. Biochem. Pharmacol 21: 2519, 1972.

3. M.R. Juchau, Q.H. Lee and P.H. Blake: Inverse correlation between aryl hydrocarbon hydroxylase activity and conversion of cholesterol to pregnenolone in human placentas at term. Life Sci. 11: 949, 1972.

4. M.R. Juchau and M.G. Pedersen: Drug biotransformation reactions in the human fetal adrenal gland. Life Sci. 12: 193, 1973.

5. M.R. Juchau and E.A. Smuckler: Subcellular localization of human placental aryl hydrocarbon hydroxylase. Toxicol. Appl. Pharmacol. (In press, 1973).

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R: REDACTED MATERIAL

Curriculum Vitae

THOMAS HILL SHEPARD May 1973

Place and Date of Birth:

Home Address: REDACTED

Marital Status:

Education:	1945	A.B. Amherst College
	1948	M.D. University of Rochester
	1946-47	Fellowship in Bacteriology and Pathology, University of Rochester
	1948-51	Clinical House Staff Training in Pediatrics
	1951-52	Chief Resident, Pediatrics, and Instructor in Pediatrics, University of Rochester
	1953	American Board of Pediatrics
	1954-55	Fellow in Endocrinology, Johns Hopkins Medical School (under Dr. Lawson Wilkins)
Military Service:	1952-54	Captain, M.C., Air Force
Positions Held:	1955-56	Instructor in Pediatrics, University of Washington, School of Medicine
	1956-61	Director of Endocrinology, Children's Orthopedic Hospital, Seattle, Washington
	1956-61	Assistant Professor of Pediatrics, University of Washington, School of Medicine
	1961-62	Research Associate in Embryology, Department of Anatomy and Visiting Assistant Professor of Pediatrics, College of Medicine, University of Florida
	1962-68	Associate Professor of Pediatrics, University of Washington, School of Medicine
	1962	Visiting Investigator, Department of Embryology, (6 mo.) Carnegie Institution of Washington, Baltimore, Maryland
	1963	Visiting Investigator, Fetal Laboratory, Department of Pediatrics (6 mo.), University of Copenhagen, Denmark
	1964-Present	Head, Central Laboratory for Human Embryology

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R: REDACTED MATERIAL

Positions Held:	1968-Present	Professor of Pediatrics, University of Washington, School of Medicine
	1967-72	Director of NIH Training Grant in Human Embryology and Teratology
	1968	President - The Teratology Society
	1970	President - Western Society for Pediatric Research
	1971-72	Bureau of Drugs, Food and Drug Administration (Consultant)
	1972-73	National Institute of Child Health and Human Development (Consultant)
	1972-73	Invited-Professor (6 mo.), Department of Pediatrics, University of Geneva
Societies:	Present	REDACTED REDACTED
Licensed:	1955	State of Washington

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PUBLICATIONS

1. Shepard TH, Clauson SW: Case of adrenogenital syndrome with hypertension treated with cortisone. Pediat. 8:805-813, Dec. 1951.

2. Wilkins L, Grumbach MM, Van Wyk JJ, Shepard TH, Papadatos C: Hermaphroditism: classification, diagnosis, selection of sex and treatment. Pediat. 16:287-299, Sept. 1955.

3. Van Wyk JJ, Grumbach MM, Shepard TH, Wilkins L: The treatment of hyperthyroidism in childhood with thiouracil drugs. Pediat. 17:221-229, Feb. 1956.

4. Shepard TH: The treatment of the adrenogenital syndrome due to adrenal hyperplasia. Bulletin of the Children's Orthopedic Hospital, Seattle, Washington. Jan. 1956.

5. Shepard TH: Carbonic anhydrase activity in blood of patients with chronic respiratory disease. Amer. J. Med. Science 233:162-166, Feb. 1957.

6. Thuline H, Shepard TH, Creighton SA: Chromosomal sex test: applications in pediatrics. A.M.A. J. Dis. Child. 94:130-136, Aug. 1957.

7. Migeon CJ, Keller AR, Lawrence B, Shepard TH: Dehydroepiandrosterone and androsterone levels in human plasma. Effect of age and sex: day-to-day and diurnal variations. J. Clin. Endocrinol. and Metabl. 17:1051-1062, Sept. 1957.

8. Datta P, Shepard TH: Carbonic anhydrase: a spectrophotometric assay. Arch. Biochem. and Biophys. 79:136-145, Jan. 1959.

9. Datta P, Shepard TH: Intracellular localization of carbonic anhydrase in rat liver and kidney tissue. Arch. Biochem. and Biophys. 81:124-129, Mar. 1959.

10. Shepard TH, Landing BH, Mason DG: Familial Addison's disease case reports of two sisters with corticoid deficiency unassociated with hypoaldosteronism. A.M.A. J. Dis. of Child. 97:154-162, Feb. 1959.

11. Shepard TH, Creighton SA, Krebs EG, Lee LW, Thuline HG: Primary hyperoxaluria I. Clinical and pathologic findings in a patient with calcium oxalate nephrocalcinosis. Pediat. 25:582-591, Apr. 1960.

12. Shepard TH, Lee LW, Krebs EG: Primary hyperoxaluria, II. Genetic studies in a family. Pediat. 25:869-871, May 1960.

13. Shepard TH, Krebs EG, Lee LW, Johnson ML: Primary hyperoxaluria, III. Nutritional and metabolic studies in a patient. Pediat. 25:1008-1017, June 1960.

14. Shepard TH, Nielsen RL, Johnson ML, Bernstein N: Human growth hormone, I. Metabolic balance studies carried out in a hypopituitary child. A.M.A. Dis. of Child. 99:74-80, Jan. 1960.

15. Shepard TH, Gartler S: Increased incidence of non-tasters of phenylthicarbamide among congenital athyreothic cretins. Science 131:929, March 1960.

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49. Shepard TH, Bass GL: Organ culture of limb buds from riboflavin-deficient and normal rat embryos in normal and riboflavin-deficient media. Teratology 3:165-167, May 1970.

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53. Hellstrom I, Hellstrom KE, Shepard TH: Cell-mediated immunity against antigens common to human colonic carcinomas and fetal gut epithelium. Int.J.Cancer 6:346-351, 1970.

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2. Shepard TH: Embryonic and fetal thyroid development in Endocrine and Metabolic Disorders in Children edited by Vincent Kelley. Paul B. Hoeber, Inc.

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R: REDACTED MATERIAL

CURRICULUM VITAE

Harvey S. Schiller, M.D.

Personal Data:

Birth Date: REDACTED
Birth Place:
Citizenship:
Marital Status:
Children:

Education:

B.S.	University of Wisconsin Madison, Wisconsin	1959-62
M.D.	Washington University St. Louis, Missouri	1962-66
Intern	Department of Pathology Yale University School of Medicine New Haven, Connecticut	1966-67
Resident; and Postdoctoral Fellow	Department of Pathology Yale University School of Medicine New Haven, Connecticut	1967-68
Postdoctoral Fellow	Department of Laboratory Medicine Yale University School of Medicine New Haven, Connecticut	1970-71

Faculty Appointments:

Chief Resident; and Instructor	Department of Laboratory Medicine Yale University School of Medicine New Haven, Connecticut	1971-72

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Faculty Appointments (Cont'd):

Assistant Professor	Departments of Laboratory Medicine and Obstetrics and Gynecology (Director, Steroid Section, Chemistry Division, Department of Laboratory Medicine) University of Washington School of Medicine Seattle, Washington	1972 - present

Military Service:

Captain, U.S. Army	Walter Reed Army Medical Center Armed Forces Institute of Pathology	1968-70

Specialty Board Certification:

Board Eligible	Anatomic and Clinical Pathology	1972

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MANUSCRIPTS IN PREPARATION

1. Cox, D., Heinrichs, W.L., Paulsen, C.A., Conrad S., Schiller, H.S., Henzl, M., and Herrmann, W.L.: Perturbations of the Human Menstrual Cycle by Oxymetholone (1973).

2. Schiller, H.S., Conrad, S., Cox, D., Heinrichs, W.L., and Herrmann, W.L.: Plasma Progesterone by Competitive Protein Binding Assay. A Comparison of Two Methods and Evaluation as an Indication of Ovulation (1973).

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R: REDACTED MATERIAL

CURRICULUM VITAE

Felix G. Freund, M.D.

Personal Data:

REDACTED

Education:

1938-41 1943 1946-48	Universidad Nacional de Buenos Aires Medical School	M.D.

Postgraduate Training:

1949-50	Hospital Fiorito, Buenos Aires	Internship	
1950-52	Hospital Fiorito, Buenos Aires	Residency	Internal Medicine
1952-54	Rawson Hospital, Buenos Aires	Residency	Anesthesiology
1954-56	Massachusetts General Hospital, Boston	Residency	Anesthesiology

Faculty Positions Held:

1957-61	Instructor in Anesthesiology, Washington University, St. Louis, Missouri
1961-63	Assistant Professor of Anesthesiology, Washington University, St. Louis, Missouri
1963-65	Instructor, Department of Anesthesiology, University of Washington School of Medicine, Seattle, Washington
1965-70	Assistant Professor, Department of Anesthesiology, University of Washington School of Medicine, Seattle, Washington
1970-	Associate Professor, Department of Anesthesiology, University of Washington School of Medicine, Seattle, Washington

Hospital Positions Held:

1950-53	Junior Member, Internal Medicine Department, Hospital Fiorito, Buenos Aires
1957-63	Assistant Anesthetist, Barnes Hospital and Children's Hospital, St. Louis Missouri
1963-	Attending staff, Department of Anesthesiology, University of Washington Medical Center and Affiliated Hospitals, Seattle

Administrative Positions Held:

1970-	Director of Clinical Services, Department of Anesthesiology, Harborview Medical Center, Seattle

Military Service:

1942 1944-45	Armed Forces of Argentina (Cavalry)

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Board Certification:

1962 Diplomate, American Board of Anesthesiology

Licensure to Practice:

1958	Iowa
1962	Missouri
1963	Washington

Organizations:

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Other Appropriate Information:

1965- Consultant to Anesthesiology Department, Group Health Hospital, Seattle, Washington

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Publications:

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19. de Jong, R.H., and Freund, F.G.: Physiology of peripheral nerve and local anesthesia. Int. Anesth. Clin. 8:35-53, 1970.

20. Freund, F.G.: Respiratory effects of subarachnoid and epidural block. Clin. Anesth. 2/1969:97-107, 1971.

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26. Freund, F.G., Martin, W.E., Wong, K.C., and Hornbein, T.F.: Abdominal rigidity induced by morphine and nitrous oxide. Anesthesiology 38:358-362, 1973.

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27. Freund, F.G. and Merati, J.K.: Errors in assessing neuromuscular blockade. Anesthesiology (in press).

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Abstracts:

1. Freund, F.G., and de Jong, R.H.: Earliest evidence of phase II myoneural block. Anesthesiology 28:250, 1967.

2. Freund, F.G., Hornbein, T.F., Martin, W.E., and Parmentier, P.: Effect of halothane and halothane-nitrous oxide on the H-reflex in man. Anesthesiology 29:191, 1968.

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R: REDACTED MATERIAL

Council for Tob. Research

CURRICULUM VITAE

Louis A. Vontver, M.D., M. Ed.

PERSONAL DATA

Citizenship	REDACTED
Date of Birth	
Place of Birth	REDACTED
Address	
	REDACTED
Marital Status	
	REDACTED

EDUCATION

High School	Powell High School Powell, Wyoming	1949-53
College	(B.A.) Magna Cum Laude University of Minnesota Minneapolis, Minnesota	1953-56
	(B.S.) Univ. of Minnesota Minneapolis, Minnesota	1956-60
Medical School	(M.D.) Univ. of Minnesota School of Medicine Minneapolis, Minnesota	1956-60
Internship	Harbor General Hospital Torrance, California	1960-61
Residency	Department of Obstetrics and Gynecology University Hospital Seattle, Washington	July 1965 - June 1969
Chief Resident	Department of Obstetrics and Gynecology University Hospital Seattle, Washington	April 1968 - March 1969
Graduate Study	(M.Ed.) Univ. of Washington Seattle, Washington	April 1969 - December 1970

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R: REDACTED MATERIAL

MILITARY SERVICE

Captain	U.S. Air Force Reserves	
Active Duty	Tachikawa Air Force Base Japan	1961-64
Active Reserves	Paine Air Force Base Washington	1964-65

RESEARCH APPOINTMENTS

Fellowship	Department of Obstetrics and Endocrinology University Hospital Seattle, Washington	1964-65

FACULTY POSITIONS

Instructor	Department of Obstetrics and Gynecology University of Washington School of Medicine	July 1969 - June 1971
Assistant Professor	Department of Obstetrics and Gynecology University of Washington School of Medicine	July 1971 - present

HOSPITAL POSITIONS

Consulting Staff at U.S. Public Health Service Hospital.
Attending Staff at University Hospital and Harborview Medical Center.
Assistant Chief, Harborview Medical Center 1972 - Present

MEDICAL LICENSURE

Minnesota (July 15, 1960)
California (November 29, 1961)
Washington (December 15, 1964)

BOARD CERTIFICATION

American Board of Obstetrics and Gynecology
November 12, 1971

PROFESSIONAL ORGANIZATIONS

REDACTED

FRATERNITIES

REDACTED

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EDUCATIONAL COMMITTEES OF UNIVERSITY OF WASHINGTON MEDICAL SCHOOL

1.	Human Biology 450 (Human Reproduction)	
	Member	1969-70
	Chairman	1970-72
2.	Test and Evaluation Committee	1969-70
3.	Curriculum Committee	1970-1972
4.	Learning Resources Advisory Committee	1971-72
5.	Ad Hoc Advisory Committee on Learning Resources in Health Sciences	1971-72

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